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K. T. S. P. Mandal's

Hutatma Rajguru Mahavidyalaya

Rajgurunagar 410 505.

Department of Zoology

T. Y. B. Sc.

ZO 353: Biological Chemistry

Semester V

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By

Prof. P. P. Shindekar

Chap. 1 "Introduction to Biochemistry"

I. The science of biochemistry.

The ultimate goal of biochemistry is to explain all life processes in molecular detail. Because life processes are performed by organic molecules the discipline of biochemistry relies heavily on fundamental principles of organic chemistry and other basic sciences. It is of no surprise that the first "biochemists" actually were organic chemists who specialized in the chemistry of compounds derived from living organisms. The text provides an historical overview of some of the key contributions of the early chemists, and of modern 20th century biochemists who have lead the discipline to where it is today. Research endeavors such as the human genome project ultimately owe their success to basic discoveries about the structure of the DNA "double helix" by Watson & Crick and the development of DNA sequencing methods by Fredrick Sanger.

II. The chemical basis of life. The biomolecules such as proteins that are present in living organisms are carbon-based compounds. Carbon is the third most abundant element in living organisms (relative abundance H > O > C > N > P > S). the 29 elements found in living organisms. The chemical reactions of biomolecules are dictated by the functional groups they contain. The general formulas of common organic compounds and functional groups that will be encountered constantly in the proteins, carbohydrates, nucleic acids and simple metabolites you will study.

III. Many biomolecules are polymers.

The principle biomolecules in cells (proteins, polysaccharides, and nucleic acids) are polymer chains of amino acids, monosaccharides, and nucleotides, respectively. Biopolymers are formed by condensation reactions in which water is removed from the reacting monomer units. Each monomer unit of a biopolymer is referred to as a residue.

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A. Proteins. Most of the chemical reactions of the cell are carried out by proteins. Proteins also are the major structural components of most cells and tissues. Proteins are often called polypeptides in reference to the fact that they are composed of amino acids held together by peptide bonds. Peptide bonds actually are amide bonds which are formed by the condensation of the carboxyl groups and amino groups of consecutive amino acids in the polymer chain. The so-called peptide backbone of a protein is a monotonous, regularly repeating structure. Projecting out from the backbone are the R-groups which are the side-chains of the amino acids. In a later chapter, we will discuss how the R-groups play a significant role in determining the 3D structure of a protein, i.e., its active conformation.

B. Enzymes: comprise one subclass of proteins. These proteins carry out chemical reactions with extraordinary specificity and speed (up to 1017-fold enhancement in reaction rate). Specificity is achieved because the binding site for reactants--the active site--is highly complementary in shape to the reactants and products. A stereo view of the active site of lysozyme. This enzyme binds to and cleaves the polysaccharide portion of the bacterial cell wall. Cleavage leads to osmotic lysis of the affected bacterium. Lysozyme is present in tears and egg whites where it helps protect against unwanted bacterial growth and infection. We will discuss the structure and function of many medically and otherwise relevant proteins and enzymes such as myoglobin, hemoglobin, collagen, trypsin, insulin receptor, glycogen phosphorylase, plasma lipoproteins, and DNA polymerase in this course. Many of these proteins and enzymes are the targets of poisons and drugs whose actions also will be discussed.

C. Polysaccharides: Polysaccharides are polymers of simple sugars known as monosaccharides (e.g., glucose). Different polysaccharides perform either structural (cellulose) or energy storage (glycogen, starch) functions. Polysaccharide and monosaccharides were some of the first biomolecules that were studied by organic chemists. You should be familiar with the different types of representations used to describe the structures of monosaccharides .A comparison of the polysaccharides starch and cellulose provides an excellent example of how structure is crucial to biological function. Namely, the structure of the glycosidic bonds linking the glucose units in cellulose and starch are very similar, yet the

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subtle difference in bond configuration determines whether the polymer is digestible (starch) or not (cellulose). We will spend a number of lectures on polysaccharide and general carbohydrate metabolism. The medical relevance of these topics cannot be overemphasized. For example, more than 1 in 30 Americans will become diabetic during their lifetimes and suffer consequences attributable to energy imbalance and monosaccharide-based tissue damage.

D. Nucleic acids. Nucleic acids are composed of nucleotide monomer units. Nucleotides themselves are composed of a monosaccharide, a nitrogenous base, and one or more phosphate groups (Fig. 1.8). The nucleotide ATP is the major energy currency of the cell which is used to power a huge variety of energy-requiring reactions. ATP and other ribonucleotides (containing ribose) also make up the biopolymer RNA. Deoxyribonucleotides (containing deoxyribose) make up DNA. All nucleotides are held together by phosphodiester linkages where one phosphate group is attached to 2 sugar units in the backbone of the polymer (Fig. 1.9). Nucleotides play key roles in information transfer in all organisms (DNA → RNA → protein). RNA also can carry out structural and enzymatic functions. For example, the formation of peptide bonds during protein synthesis actually is performed by one of the RNA constituents of the ribosome. In addition the main structural component of ribosomes is RNA. Lastly, a number of nucleic acid analogs are used to inhibit DNA synthesis and are extremely important in management of cancers and virally caused diseases such as AIDS.

E. Lipids: Lipids are a diverse collection of biomolecules that are composed mostly of carbon and hydrogen, i.e., hydrocarbons. Lipids contain relatively few polar functional groups. They typically are more soluble in organic solvents than in water. The primary building block of many lipids is a fatty acid. The most common structural lipid in cell membranes--glycerophospholipid- -contains 2 fatty acids, glycerol and a polar head group (Fig. 1.11 & 1.12). When collected as assemblies of millions of molecules, the classical biological structure known as a membrane is formed (Fig. 1.13). Biological membranes usually contain proteins, and protein content and composition is highly variable and determined by membrane function. Although discussed here along with true biopolymers, membranes are actually molecular aggregates. In later chapters, we will cover the functions of membrane-bound proteins, enzymes and receptors. We'll discuss how membranes serve as the primary sites of energy production in aerobic tissues such as the brain and liver,

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how membrane-bound hormone receptors signal metabolic changes in cells, and how many toxins act to impair membrane protein function

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